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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: David Stern, et al.

Serial No.: 09/374,213

Filed : August 13, 1999

For : METHODS OF INHIBITING BINDING OF  $\beta$ -SHEET FIBRIL  
TO RAGE AND CONSEQUENCES THEREOF



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1185 Avenue of the Americas  
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December 23, 1999

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following references which are listed on the PTO-1449 form attached hereto as **Exhibit A**. Copies of these references are attached hereto as **Exhibits 1-25** respectively.

1. Akama, T. Keith, et al., (1998) "Amyloid  $\beta$ -peptide stimulates nitric oxide production in astrocytes through an NgkB-dependent mechanism," Proc. Natl. Acad. Sci. 95:5795-5800 (**Exhibit 1**);
2. Behl, C., et al., (1994) "Hydrogen Peroxide Mediates Amyloid  $\beta$  Protein Toxicity," Cell 77:817-827 (**Exhibit 2**);
3. Combs, K. Colin, et al. (1999) "Identification of Microglial Signal Transduction Pathways Mediating a Neurotoxic Response to Amyloidogenic Fragments of  $\beta$ -Amyloid and Prion Proteins," Journal of Neuroscience 19(3)928-939 (**Exhibit 3**);

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4. Forloni, Gianluigi, et al. (1996) "Amyloid in Alzheimer's Disease and Prior-Related Encephalopathies: Studies With Synthetic Peptides," Progress in Neurobiology 49:287-315 (Exhibit 4);
5. Ghiso, Jorge, et al. (1994) "Unifying Features of Systemic and Cerebral Amyloidosis," Molecular Neurobiology 8(1) 49-64 (Exhibit 5);
6. Inagaki, Fuyuhiko, et al. (1978) "Conformation of Erabutoxins a and b in Aqueous Solution as Studied by Nuclear Magnetic Resonance and Circular Dichroism," 89:433-443 (Exhibit 6);
7. Kimball, M.R., et al. (1979) "Molecular Conformation of Erabutoxin b; Atomic Coordinates At 2.5 Å Resolution," Biochemical and Biophysical Research Communications 88:950-959 (Exhibit 7);
8. Kindy, S. Mark and Rader, J. Daniel (1998) "Reduction in Amyloid A Amyloid Formation in Apolipoprotein-E-Deficient Mice," American Journal of Pathology 152:1387-1395 (Exhibit 8);
9. Kirschner, A. Daniel, et al. (1986) "X-ray diffraction from intraneuronal pairs helical filaments and extraneuronal amyloid fibers in Alzheimer disease indicates cross- $\beta$  conformation" Proc. of the National Academy of Sciences 83:503-507 (Exhibit 9);
10. Kilsilevsky, Robert, et al. (1995) "Arresting amyloidosis in vivo using small-molecule anionic sulphonates or sulphates: implications for Alzheimer's disease," Nature Medicine 1:143-148 (Exhibit 10);

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11. Lander, M. Harry, et al. (1997) "Activation of the Receptor for Advanced Glycation End Products Triggers a p21<sup>ras</sup>-dependent Mitogen-activated Protein Kinase Pathway Regulated by Oxidant Stress," Journal of Biological Chemistry 272:17810-17814 (**Exhibit 11**);
12. Levine, Harry (1993) "Thioflavine T interaction with synthetic Alzheimer's disease  $\beta$ -amyloid peptides: Detection of amyloid aggregation in solution," Protein Science 2(3):404-410 (**Exhibit 12**);
13. Mattson, P. Mark and Goodman, Yadong (1995) "Different amyloidogenic peptides share a similar mechanism of neurotoxicity involving reactive oxygen species and calcium," Brain Research 676(1):219-224 (**Exhibit 13**);
14. Pike, J. Christian, et al. (1993) "Neurodegeneration Induced by  $\beta$ -Amyloid Peptides in vitro: The Role of Peptide Assembly State," Journal of Neuroscience 13(4):1676-1687 (**Exhibit 14**);
15. Prusiner, B. Stanley, et al. (1998) "Prion Protein Biology," Cell 93:337-348 (**Exhibit 15**);
16. Serpell, L.C., et al. (1997) "The molecular basis of amyloidosis," Cellular and Molecular Life Sciences 53:871-887 (**Exhibit 16**);
17. Sipe, D. Jean, et al. (1993) "Characterization of the Inbred CE/J Mouse Strain as Amyloid Resistant," American Journal of Pathology 143:1480-1485 (**Exhibit 17**);
18. Sipe, D. Jean (1992) "Amyloidosis," Annual. Review of

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Biochemistry 61:947-975 (**Exhibit 18**);

19. Smith, A. Mark, et al. (1994) "Heme Oxygenase-1 is Associated with the Neurofibrillary Pathology of Alzheimer's Diseases," American Journal of Pathology 145:42-47 (**Exhibit 19**);
20. Soto, Claudio and Castano, M. Eduardo (1996) "The conformation of Alzheimer's  $\beta$  peptide determines the rate of amyloid formation and its resistance to proteolysis," Biochemical Journal 314:701-707 (**Exhibit 20**);
21. Soto, Claudio, et al. (1995) "Apolipoprotein E increases the fibrillogenic potential of synthetic peptides derived from Alzheimer's, Gelsolin and AA amyloids," FEBS Letters 371:110-114 (**Exhibit 21**);
22. Strauss, Sylvia, et al. (1992) "Detection of Interleukin-6 and  $\alpha_2$ -Macroglobulin Immunoreactivity in Cortex and Hippocampus of Alzheimer's Disease Patients," Journal of the Academy of Pathology 66(2):223-230 (**Exhibit 22**);
23. Yan, Shi Du, et al. (1997) "Amyloid- $\beta$  peptide-Receptor for Advanced Glycation End product interaction elicits neuronal expression of macrophage-colony stimulating factor: A proinflammatory pathway in Alzheimer disease," Proceedings of the National Academy of Sciences 94:5296-5301 (**Exhibit 23**);
24. Yan, Shi Du, et al. (1996) "Rage and amyloid- $\beta$  peptide neurotoxicity in Alzheimer's disease," Nature 382:685-691 (**Exhibit 24**); and
25. Yankner, A. Bruce (1996) "Mechanisms of Neuronal

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Degeneration in Alzheimer's Disease," Neuron 16:921-932  
(Exhibit 25)

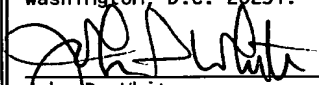
If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone at the number provided below.

Pursuant to 37 C.F.R. §1.97(b)(3), no fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this paper is being deposited this date with the U.S. Postal Service as first class mail addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.	
 John P. White Reg. No. 28,678	12/23/99 Date